

Dr. Wendling, *et al* reply

To the Editor:

We read with interest the comment by Nagashima and Minota about our editorial¹. We had mentioned the very interesting paper of our Japanese colleagues, reporting the first case of HBsAg-positive RA patient treated more than 5 years with an anti-interleukin 6 receptor monoclonal antibody (tocilizumab)². Indeed, antiviral therapy (entecavir) was added after 7 years of tocilizumab therapy. It is noteworthy, even if the patient was retrospectively diagnosed as HBsAg-positive with high viral load before starting tocilizumab, that there was no evidence of exacerbation of hepatitis during these years of tocilizumab treatment, even without antiviral therapy for more than 5 years. This is of interest because interleukin 6 reduces HBV replication³, and tocilizumab may be able to reactivate viral infection, such as Epstein-Barr virus⁴.

This isolated and exceptional case is, of course, not a proof of safety of tocilizumab in every HBsAg-positive carrier, and we fully agree with the concluding comments of Nagashima and Minota, concordant with our previous statements about biologic agent use in this situation⁵. The longterm effects of antiviral therapy are unknown, and mutations and acquired resistance may occur, as shown in some cases with anti-tumor necrosis factor (anti-TNF) treatment in HBsAg-positive patients⁶. These considerations emphasize the need for systematic screening for HBV status in rheumatic diseases before starting biologic therapy with anti-TNF agents⁷, rituximab⁸, and abatacept⁹; this is also the case for tocilizumab.

International guidelines¹⁰ suggest that in HBsAg-positive patients, when immunosuppressive therapy is indicated, a preemptive treatment with lamivudine, entecavir, or tenofovir is required to prevent viral reactivation. This preemptive therapy should be given 7 days prior and maintained as long as the immunosuppressive treatment is present, and for 6 months after cessation. Tight control of transaminases and viral load is mandatory during treatment, and at least 3 months after discontinuation of the immunosuppressive agent.

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REFERENCES

1. Wendling D, Di Martino V, Herbein G. Biologic agents in the treatment of rheumatic diseases with chronic viral infection. Where are we? [editorial]. *J Rheumatol* 2009;36:1107-8.
2. Nagashima T, Minota S. Long-term tocilizumab therapy in a patient with rheumatoid arthritis and chronic hepatitis B. *Rheumatology* 2008;47:1838-40.
3. Kuo TM, Hu CP, Chen YL, Hong MH, Jeng KS, Liang CC, et al. HBV replication is significantly reduced by IL-6. *J Biomed Sci* 2009;16:41.
4. Ogawa J, Harigai M, Akashi T, Nagasaka K, Suzuki F, Tominaga S, et al. Exacerbation of chronic active Epstein-Barr virus infection in a patient with rheumatoid arthritis receiving humanised anti-interleukin-6 receptor monoclonal antibody. *Ann Rheum Dis* 2006;65:1667-9.
5. Wendling D, Herbein G. TNF-alpha antagonist therapy in patients with joint disease and chronic viral infection. *Joint Bone Spine* 2007;74:407-9.
6. Wendling D, Di Martino V, Prati C, Toussierot E, Herbein G. Spondyloarthritis and chronic B hepatitis. Effect of anti-TNF therapy. *Joint Bone Spine* 2009;76:308-11.
7. Furst DE, Keystone EC, Kirkham B, Kavanaugh A, Fleischmann R, Mease P, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2008. *Ann Rheum Dis* 2008;67 Suppl 3:iii2-25.
8. Pham T, Fautrel B, Gottenberg JE, Goupille P, Hachulla E, Masson C, et al. Rituximab (MabThera) therapy and safety management. Clinical tool guide. *Joint Bone Spine* 2008;75 Suppl 1:S1-99.
9. Pham T, Claudepierre P, Constantin A, Fautrel B, Gossec L, Gottenberg JE, et al. Abatacept therapy and safety management. *Joint Bone Spine* 2009;76 Suppl 1:S3-S55.
10. Barclay S, Pol S, Mutimer D, Benhamou Y, Mills PR, Hayes PC, et al. The management of chronic hepatitis B in the immunocompromised patient: Recommendations from a single topic meeting. *J Clin Virol* 2008;42:104-15.

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